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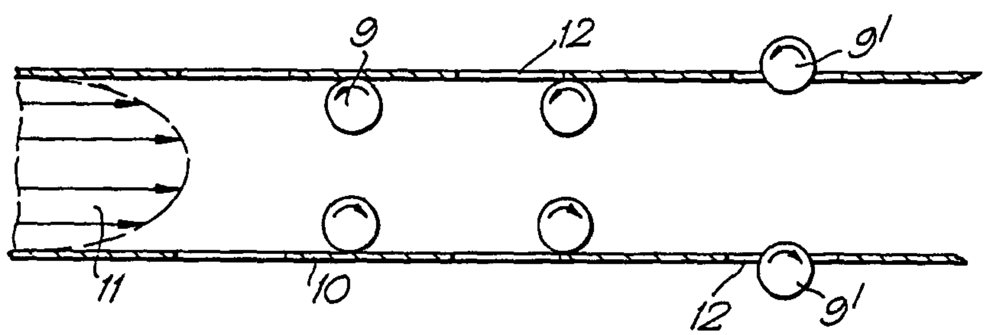

(57) Abstract

A method and apparatus for separating discoid particles (9) from particles of comparable size and different shape, wherein a mixture of the particles in a fluid matrix is caused to flow in a conduit alongside a wall (10) formed with slits (12) extending substantially parallel to the direction of flow, whereby at least a proportion of the discoid particles migrate to and roll along the slit wall and are washed out of the conduit through the slits.

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DESCRIPTION

PARTICLE SEPARATION

Significant problems exist in separating particles of similar size and density, particularly when the maximum dimensions of the particles are of the order of a few microns, as is the case with blood components. Even when the particles are of different average sizes, filtration through a filter of appropriate pore size is generally inadequate because it is very difficult to make filter membranes with a uniform pore size and consequently there is a diffuse cut-off in the particle classification, amounting to as much as a factor of ten in variation in the size of particles in the filtrate. This is exacerbated by the tendency for the particles, which are just too large to pass through the filter pores, to settle in and block the pores.

The inventor's recent experiments indicate that, contrary to previous general understanding, discoid particles carried by a fluid matrix flowing parallel to a surface tend to migrate to the surface and to align themselves with their planes parallel to the flow direction and perpendicular to the adjacent surface, i.e. they roll along the surface. This appears to be a result of the frictional interaction between the particles and the shear flow which inherently occurs when liquid flows adjacent to a surface owing to the drag which the surface applies to the immediately adjacent fluid boundary layer.

It is now appreciated that if the surface, towards which the discoid particles migrate is provided with slits of an appropriate size extending in the direction of flow, so that the discoid particles can pass out through the slits, this would provide a possible way of separating discoid

particles from fatter particles of similar size.

In accordance with the present invention, therefore, in a method of separating discoid particles from particles of comparible size but different shape, a mixture of the particles in a fluid matrix is caused to flow along a conduit having a wall formed with slits extending substantially parallel to the direction of flow, whereby at least a proportion of the discoid particles migrate to and roll along the slit wall and are washed out of the conduit through the slits.

The new method thus involves filtration by size, shape and orientation, rather than merely by size and it is believed that this will lead to a superior separation technique where discoid particles are involved. The width and length of the slits will of course be selected in dependence upon the average width and diameter of the discoid particles to be separated. For example, the width of the slits will normally be greater than the width, but less than the diameter, of the discoid particles.

For large particles, the slits may be cut in a membrane or other wall of the conduit. However, where particles of the size of the order of a few microns are involved, it may be suitable to use as the conduit wall a porous membrane which has been subjected to bi-axial stretching, i.e. perforated and stretched, if necessary after heating, so that its pores become elongate. Examples of such membranes are Goretex (PTFE) and Celgard (polypropylene).

In as much as the migration and orientation of the discoid particles depends upon the shear flow of the carrier fluid, it is preferred if the fluid is flushed to and fro alongside the wall so that the r peat d deceleration and accel ration maximizes the sh ar affect. This may be achiev d by diaphragm or other pumps working out of phase at respective ends

Non medical applications involve the possible separation of plant or animal cells in a bio-reactor.

The invention also includes apparatus for carrying out the new method the apparatus comprising a conduit at least partly defined by a wall provided with substantially parallel slits, and means for causing a fluid in the conduit to flow alongside the slit wall with a major component substantially parallel to the lengths of the slits.

The invention is illustrated diagrammatically in the accompanying drawing, in which:-

Figure 1 is a diagramatic representation of the principle behind the invention;

Figure 2 is a diagramatic perspective view of apparatus according to the invention;

Figure 3 is a section taken on the line III-III in Figure 2;

Figure 4 is a section taken on the line IV-IV in Figure 2;

Figure 5 is a section taken on the line V-V in Figure 2;

Figure 6 is an enlarged portion of Figure 4;

Figure 7 is an axial section through an alternative apparatus in accordance with the invention; and,

Figure 8 is a flow diagram showing a possible use of the apparatus.

Figure 1 represents the flow of discoid particles 9, and other particles, along a conduit 10 in a shear flow as representated at 11, i.e. the flow velocity is less adjacent to the walls of the conduit than along the centre of the conduit with a graded velocity between. According to the inventor's theory, this causes the discoid particles 9 to stand up on, and roll along, the walls 10 as shown. If slits 12, the lengths of which extend along the conduit, and having a length somewhat greater than

the diam t r of the discoid particles 9, are provided in the walls 10, some of the discoid particles can be persuaded to pass out of the conduit throught the slits as indicated at 9'.

One separating apparatus which is arranged to take advantage of this phenomenon is illustrated in Figures 2 to 6. As shown in Figure 2, a separator 13 is carried face to face by an upright wall 14 and consists of similar opposed side plates 15 and similar pairs of end plates 16 and 17. The side plates 15 are rectangular and elongate and the facing adjacent surfaces of these plates are profiled. Positioned between the two profiled surfaces of the side plates 15 are a pair of membranes 18. Along the longer sides of the plates 15, the membranes 18 are sealed to one another and to the plates 15 by clamping bolts 19, which draw the plates together, and pairs of sealing beads 20, which are seated in grooves in the plates 15, and abut the membranes 18. The profiling of the facing surfaces of the plates 15 involve a series of parallel ribs 21, which extend parallel to the longer dimension of the plates 15. There is thus formed between the membranes 18, a central primary conduit 22 and, between each membrane 18 and the adjacent profiled surface of the adjacent plate 15, a secondary conduit 23. At intervals along the longer dimension of the plates 15, their profiled surfaces are provided with transverse channels 24, which intersect the grooves between the ribs 21, and ensure complete irrigation of the secondary conduits between the membranes and profiled faces of the plates 15.

At each of the ends of the plates 15, two plates 16 and 17 are bolted to them by bolts 25 and the ends of the membranes 18 are clamped between the ends of the plates 15 and the end plates 16. Clamped b tween each of the plates 16 and the adjacent plate

17, is it an outwardly extending flange 26 of a flexible diaphragm 27. A manifold 28, in communication with the adjacent end of the primary conduit 22, is formed within an open interior of the plate 16 and each of these manifolds 28 is connected through a bore 28' with an external nipple and hose 29, 29'. The diaphragms 27 are accommodated within openings within the respective plates 17 and are acted upon by respective pushers 30, 30' carried by arms 31, 31', which work through elongate slots 32, 32' in the board 14, and carried on respective ends of a member 33. This member is reciprocable in a linear bearing 34 by means of a motor 35 acting through a crank 36. As the member 33 is moved to and fro liquid is flushed to and fro through the primary conduit 22. However, the stroke of the pusher 30 extends further into the respective plate 17 than does the pusher 30', as a result of which there is superimposed upon the reciprocating flow in the primary conduit 22, a component which provides a net mean flow from the inlet hose 29 to the outlet hose 29'.

At one end of the plates 15, each of the secondary conduits 23 and one of the channels 24 communicate through a port 37 in the respective plate via a bore 38 in the respective plate, with a nipple and hose 39.

As suggested in Figure 6, each of the membranes 18 is provided with a large number of slits extending parallel to the lengths of the plates 15. The slits may have any appropriate length, e.g. of the order of a few microns upwards, depending upon the dimensions of the discoid particles to be separated.

When a fluid matrix containing discoid and fatter particles of similar dimensions is supplied to the primary conduit 22 through the hose 29, and the mixture is flushed to and fro within the conduit 22,

but with a mean flow along the conduit 22, the discoid particles will roll along the membranes 18 analogously to what is shown in Figure 1. Discoid particles will pass through the slits into the secondary conduits 23 and hence may be collected by withdrawal through the hoses 39 to which a suction may need to be applied unless the fluid in the conduit 22 is under a pressure of say a head of up to 1m. The residue of this filtration is withdrawn through the hose 29'.

Figure 7 shows very diagrammatically an alternative seperator consisting of a stationary inner cylindrical member 40 having a cage 41 covered by a membrane 42. The cage is rigid at its top with a fixed bar 43 and has at the bottom an outlet pipe 44 passing through a fixed collar 45. The inner cylindrical member is surrounded by an outer cylindrical wall 46 having radially inwardly extending end walls 47, the radially inner edges of which are rotatably and slidingly sealed to the ends of the inner member 40. The wall 46 is provided with flexible inlet and outlet hoses 48 and 49, and is rotatably mounted in bearings 50. A yoke 51 is fixed to the upper wall 47 and straddles the bar 43. The yoke 50 is fixed to a shaft 52, supported in a bearing 53 and connected via a crank 54 to a motor 55. When the motor is operated, the shaft 52, yoke 51, and walls 46 and 47 are oscillated to and fro through a small angle such that the bar 43 does not interfere with the yoke 51.

The apparatus of Figure 7 is analogous to that of Figures 2 to 6 in that oscillatory shear flow is provided within an annular conduit 56 between the wall 46 and membrane 42, in practice with a superimposed small axial mean flow from the inlet 48 to the outlet 49. If then a mixture of discoid and other fatter particles of similar dimensions in a

fluid matrix is introduced into the annular chamb r 56 through the inlet 48, the discoid particles will tend to migrate down the velocity gradient to the membrane 42 and stand up in a sense to roll around the membrane circumferentially. The membrane 42 is provided with slits extending circumferentially of the member 40 so that the discoid particles will tend to pass through the slits into the interior of the member 40 and hence out through the hollow shaft 44. The residue of this filtration will eventually pass out of the outlet 49.

Typical dimensions for the Figure 7 apparatus might be an internal diameter of the wall 46 of 100 mm and a radial spacing between the member 40 and the wall 46 of 2.5 mm.

Figure 8 illustrates how the invention might be used in practice. Thus whole blood would be drawn from a patient P and plasma filtered off in a plasmapheresis device 57, which might be constructed as that described in EP-A-0111423. The plasma-free whole blood is then diluted with saline from a source 58 and fed to an apparatus 59 as previously described. In this apparatus the membrane slits would be dimensioned to allow the filtering of good discoid red cells, sickle cells being rejected and passing out along a line 60. The good cells and saline will then be reconcentrated in a device 61, reunited with the previously filtered out plasma in the device 62, and reinfused back into the blood stream of the patient P.

CLAIMS

1. A method of separating discoid particles (9) from particles of comparable size but different shape, wherein a mixture of the particles in a fluid matrix is caused to flow in a conduit (22,56) alongside a wall (11,18,42) formed with slits (12) extending substantially parallel to the direction of flow, whereby at least a proportion of the discoid particles migrate to and roll along the slit wall and are washed out of the conduit through the slits.

2. A method according to claim 1, in which the mixture of the particles in the fluid matrix is flushed to and fro alongside the wall.

3. A method according to claim 2, in which the flushing to and fro is achieved by pumps (27) working out of phase at respective ends of the conduit.

4. A method according to claim 2, in which the flushing is achieved by relative reciprocation or oscillation of opposed walls (42, 46) defining the conduit, at least one of which walls is provided with the slits.

5. A method according to any one of the preceding claims, which is operated continuously, the conduit being fed with make-up mixture which exceeds the loss of filtrate from the conduit so that there is a mean flow along the conduit.

6. A method according to any one of the preceding claims, in which the discoid particles are blood platelets or blood red cells.

7. Apparatus for carrying out the method according

to any one of the preceding claims, the apparatus comprising a conduit (22,56) at least partly defined by a wall provided with substantially parallel slits, and means (27,55) for causing a fluid in the conduit to flow alongside the slit wall with a major component substantially parallel to the lengths of the slits.

8. Apparatus according to claim 7, in which the flow producing means is arranged to cause the fluid to flush to and fro alongside the slit wall.

9. Apparatus according to claim 8, in which the flow producing means comprises pumps (27) operating out of phase at opposite ends of the chamber or conduit.

10. Apparatus according to claim 8 , in which the flow producing means comprises means (54,55) for relatively reciprocating or oscillating opposed walls of the conduit, of which at least one of the walls is the slit wall.

Fig.1.

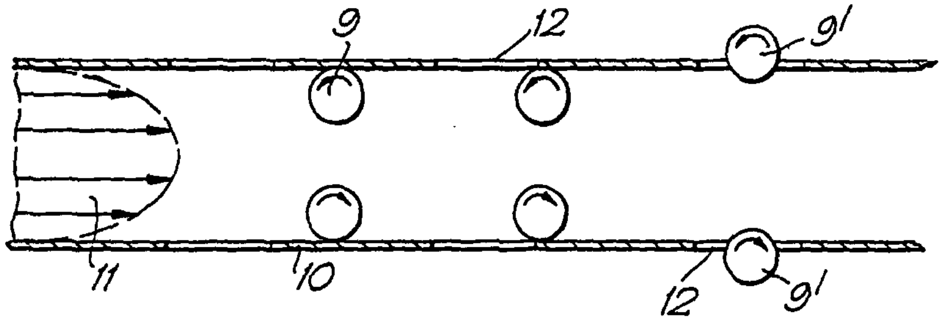

Fig.4.

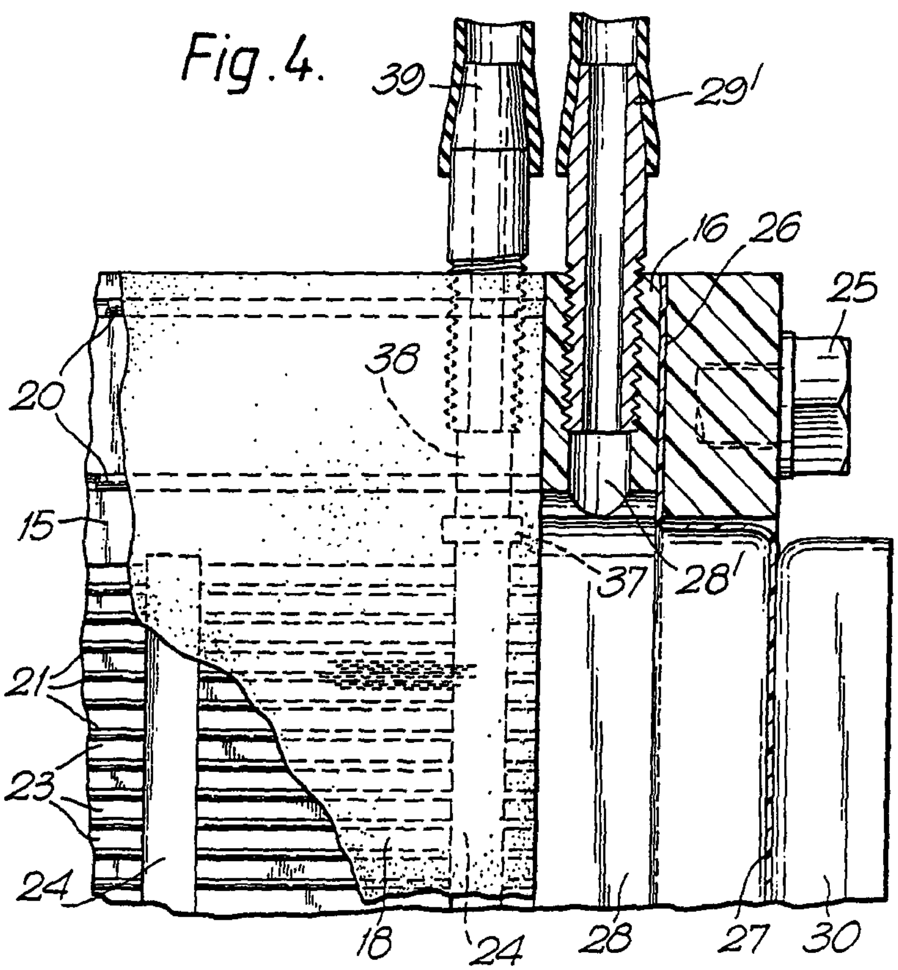

Fig.2.

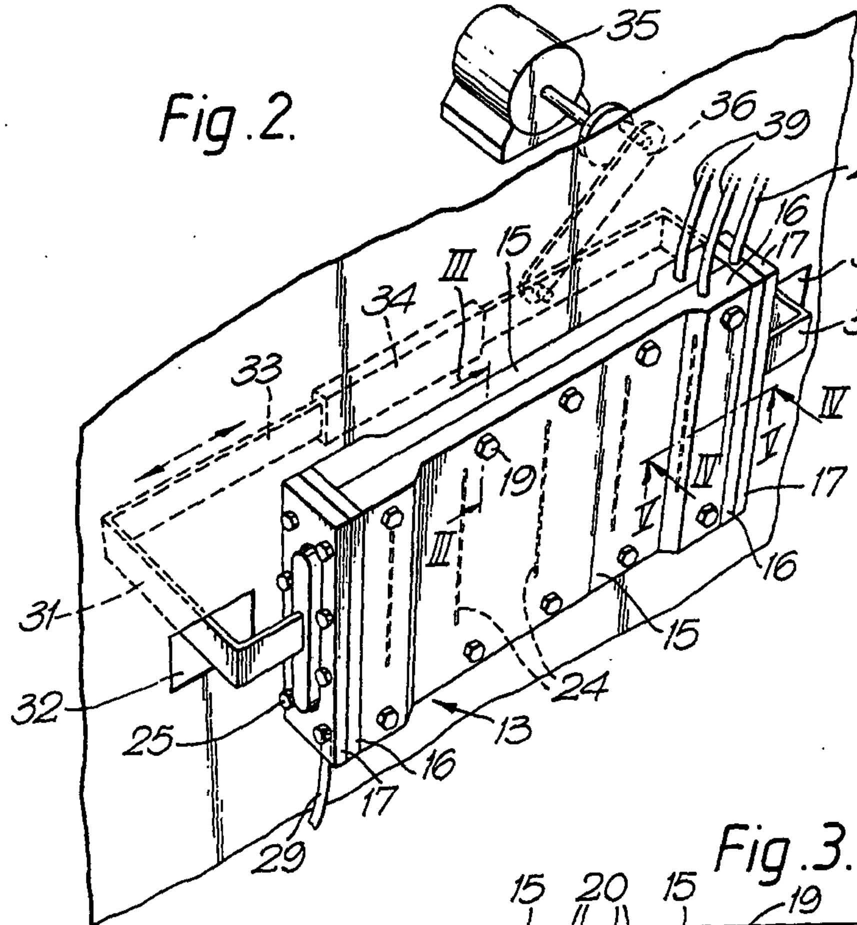
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Fig.3.

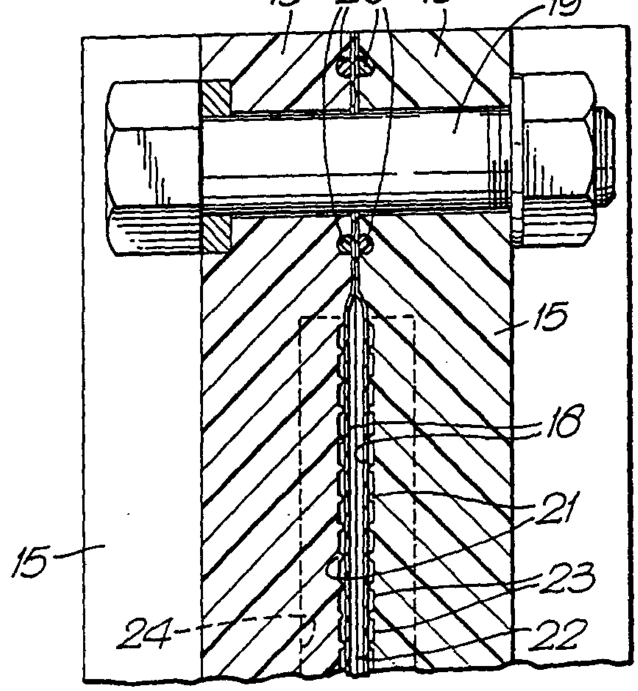
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Fig. 5.

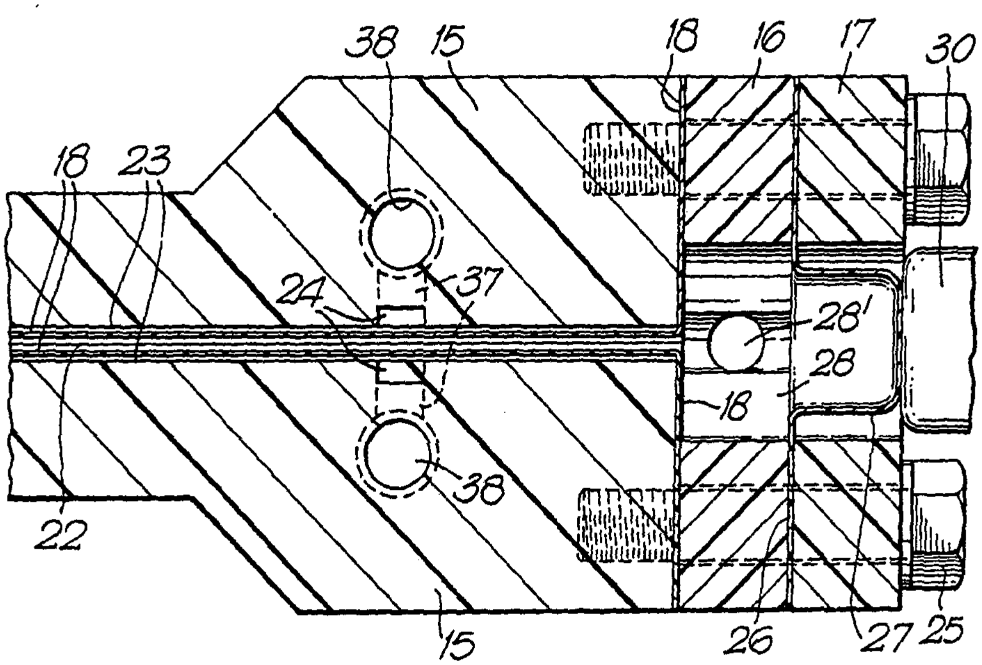


Fig. 7.

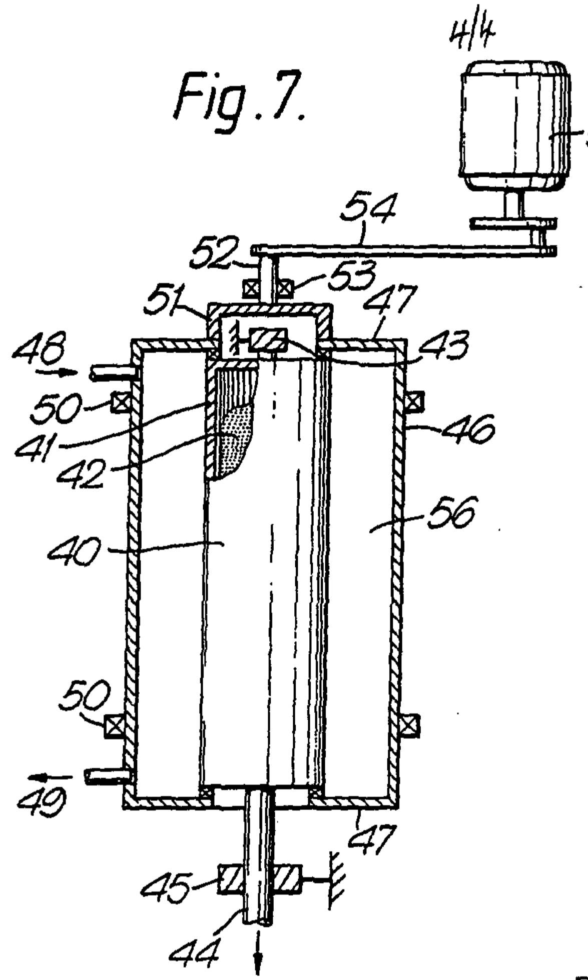


Fig. 6.

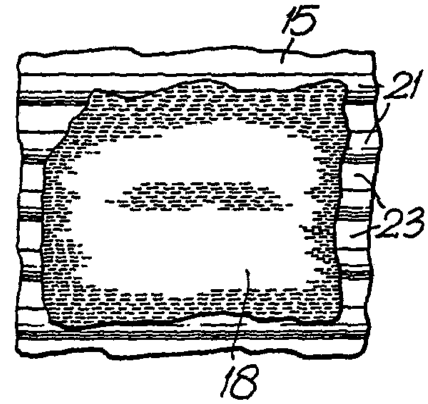
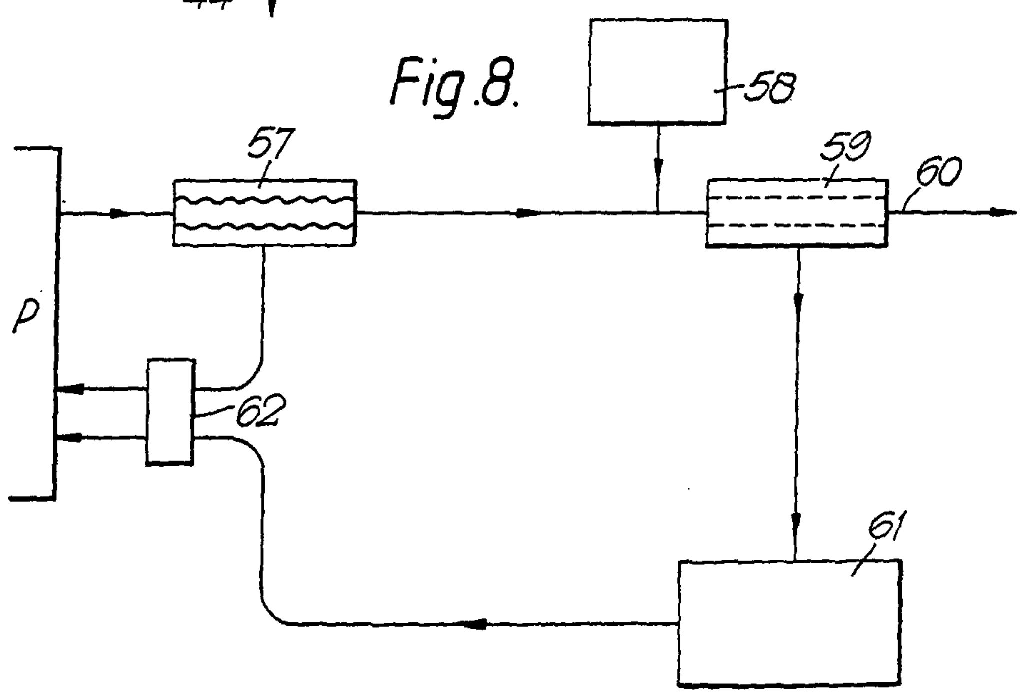


Fig. 8.



INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 87/00865

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC4: A 61 M 1/34; B 01 D 13/00; G 01 N 33/48

II. FIELDS SEARCHED

Minimum Documentation Searched

Classification System	Classification Symbols
IPC4	A 61 M; A 61 K; B 07 B; G 01 N

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched

III. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
A	US, A, 3231087 (CUSI) 25 January 1966, see column 2, line 21 - column 3, line 48; figures 1-6	1,7
A	CH, A, 506331 (LONZA) 15 June 1971, see column 1, lines 26-34; column 3, lines 49-57	1,5,7
A	Transactions/American Soc. for Artificial Internal Organs, vol. XXVII, 1981, (Washington, DC, US), B.A. Solomon: "Membrane separations: technological principles and issues", pages 345-350, see page 345, lines 36-46	1
A	Life Support Systems, vol. 4, no. 3, July-September 1986 (London, GB), J.W. Stairmand et al.: "Separation of plasma from whole blood by membrane filtration in oscillatory flows", pages 193-204, see page 196, lines 3-8; figure 3	2-4,8-10

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
1st March 1988	07 APR 1988
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	P.C.G. VAN DER PUTTEN

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. GB 8700865

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A- 3231087		None	
CH-A- 506331	30-04-71	None	

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